

## **REMARKS**

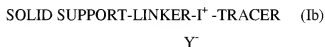
### **I. Amendment to the Claims**

No amendments to the claims have been made. Claims 4 and 15 are pending.

### **II. Rejection under 35 U.S.C. § 103(a)**

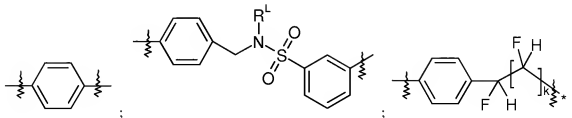
Claims 4 and 15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Luthra et al (US 2004/0236085) ("Luthra") in view of Stevens et al. (WO01/14354) ("Stevens") and Scheler (US 4,540,648) ("Scheler"). Applicants respectfully disagree and traverse the rejection.

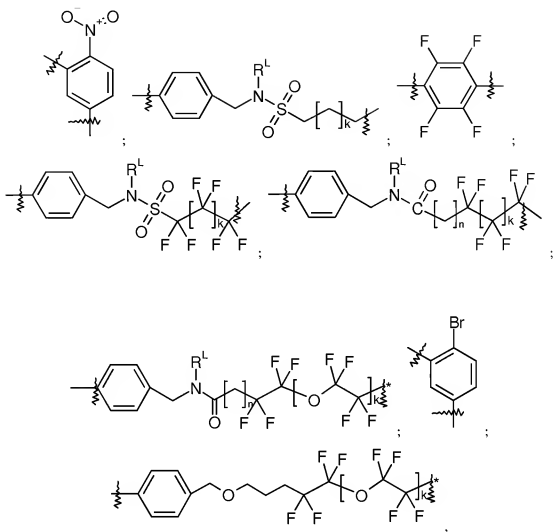
Applicants' claimed invention is directed to a process for the production of an  $^{18}\text{F}$ -labelled tracer which comprises treatment of a solid support-bound precursor of formula (Ib):



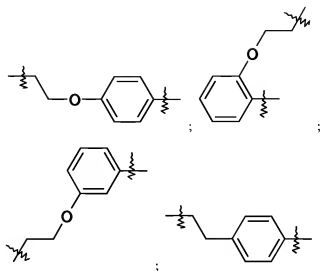
wherein:

- (a)  $\text{Y}^-$  is an anion,
- (b) the SOLID SUPPORT is a polymer selected from polystyrene which is optionally block grafted, polyacrylamide, and polypropylene or glass or silicon coated with such a polymer,
- (c) the LINKER is selected from:



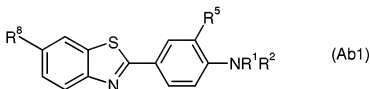


wherein at each occurrence, k is an integer of 0 to 3, n is an integer of 1 to 16, and  $\text{R}^{\text{L}}$  is hydrogen or C1-6alkyl; and



wherein each phenyl ring is optionally substituted by 1 to 4 groups selected from C<sub>1-6</sub>alkyl and C<sub>1-6</sub>alkoxy; and

(d) the TRACER is of formula (Ab1)



wherein:

R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> haloalkyl, and a protecting group selected from alkoxycarbonyl;

R<sup>5</sup> is hydrogen, C<sub>1-6</sub> alkyl, or a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup> group in formula (Ib);

R<sup>8</sup> is hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> alkyl, or a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup> group in formula (Ib);

provided that only one of R<sup>5</sup> and R<sup>8</sup> is a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup> group in formula (Ib);

with <sup>18</sup>F<sup>-</sup> to produce the labelled tracer of formula (IIb);

<sup>18</sup>F-TRACER (IIb)

wherein the TRACER is as defined for the compound of formula (Ib) except that one of R<sup>5</sup> and R<sup>8</sup> is a bond to the <sup>18</sup>F instead of a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup> group in formula (Ib);

optionally followed by:

- (i) removal of excess <sup>18</sup>F<sup>-</sup>; and/or
- (ii) removal of any protecting groups; and/or
- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound of formula (IIb) as an aqueous solution.

More simply, Applicants' claimed invention is directed to a regiospecific solid-phase <sup>18</sup>F-fluorination process of benzothiazole compounds. Specifically, according to Applicants' claimed invention, the TRACER of formula (Ab1) is labeled with <sup>18</sup>F at either the R<sup>5</sup> or R<sup>8</sup> position. As recognized by the Examiner, Luthra fails to teach or suggest the labeling of benzothiazole compounds, much less the regiospecific labeling of benzothiazole compounds. Hence Luthra fails to teach or suggest Applicant's claimed regiospecific benzothiazole <sup>18</sup>F-labeling process.

Stevens and Scheler are relied upon for their description of benzothiazole compounds. Stevens describes that their <sup>18</sup>F labeled compounds are prepared from the corresponding iodo substituted compound (Stevens, page 5, lns. 13-17). More simply, Stevens describes a nucleophilic displacement process of an iodo group with <sup>18</sup>F<sup>-</sup>. None of the "Preparative Methods" set forth on pages 15-20 of Stevens teach or suggest a solid-phase <sup>18</sup>F-fluorination process of benzothiazole compounds. Example 45 on page 40 of Stevens is the only radiofluorination example and it also does not teach or suggest a solid-phase <sup>18</sup>F-fluorination process of benzothiazole compounds but rather a (i) displacement reaction using the corresponding iodo-substituted precursor compound and (ii) a "regiospecific cyclisation" route. Since Stevens provides no teaching or suggestion of a solid-phase, regiospecific <sup>18</sup>F-fluorination process of benzothiazole compounds, it does remedy the deficiencies of Luthra and hence does not render Applicants' claimed invention obvious.

Scheler described a non-halogenated benzothiazole compound of formula (I) for use as a light absorbing compound (*see* Col. 3, Ins. 25-40). The “support” of Scheler is what a “light sensitive layer” lies upon (*see* Col. 7, Ins. 6-66 and claim 1) and is not the solid support of Applicants’ claimed invention to which the LINKER is covalently bound (*see* definition of “SOLID SUPPORT” on page 6, Ins. 1-3 of Applicants’ Specification). Further Scheler is silent as to radioisotopic compounds. Scheler is silent as to solid phase synthesis of radioisotopic compounds. Scheler is wholly unconcerned with radiofluorination of benzothiazole compounds. Since Scheler provides no teaching or suggestion of a solid-phase, regiospecific <sup>18</sup>F-fluorination process of benzothiazole compounds, it does remedy the deficiencies of Luthra or Stevens and hence does not render Applicants’ claimed invention obvious.

None of the references whether alone or in combination would teach or suggest Applicant’s claimed invention. Applicants’ claimed invention is not obvious in view of the cited references. Applicants respectfully request this rejection be withdrawn.

### III. Conclusion

In view of the remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has now been successfully overcome or obviated, and that all the pending claims are now in condition for allowance. Withdrawal of the Examiner’s rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Appl. No. 10/539,169  
Amdt. Dated  
Reply to Office action of February 2, 2011

The Director is hereby authorized to charge any fees due in connection with this  
Amendment against Deposit account number 502-665.

Respectfully submitted,

/Christine S. Lee/

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